Magnesium and calcium excretion during pregnancy

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Zusammenfassung

Zur Untersuchung der Gründe des Absinkens des Magnesiumplasmagehaltes (Mg) in der Schwangerschaft, von dem gezeigt werden konnte, daß er mit einer Erniedrigung des Mg-Spiegels im Myometrium korreliert, sollte die Mg- und Kalziumausscheidung (Ca) im Urin in der Schwangerschaft bestimmt werden. Es wurde bei sieben Probandinnen während der Schwangerschaft in vierzehntägigen Abständen 24-Stunden-Urin gesammelt und Blut entnommen. Im Urin und Plasma wurde Mg mit Atomabsorptionspektrophotometrie und Ca colorimetrisch bestimmt. Die Clearances wurden errechnet. Es zeigte sich eine 25%ige Erhöhung der Mg-Ausscheidung auf 4,78 mmol/24 h ($p<0,05$). Der Mg-Plasmawert sank um 25 % auf 0,70 mmol/l ($p<0,01$). Die Mg-Clearence wurde um 41 % auf 4,57 ml/min erhöht ($p<0,05$). Schon im ersten Trimenon ist die Ca-Ausscheidung um 41 % auf 4,86 mmol/24 h angestiegen ($p<0,05$). Die Ca-Plasmakonzentration fällt um 12 % auf 2,16 mmol/l ($p<0,001$). Die Ca-Clearance steigt um 123 % auf 2,03 ml/min an ($p<0,02$). Somit ist wahrscheinlich die Erhöhung der Mg-Ausscheidung im Urin für eine Mg-Mangelsituation mitverantwortlich. Für die relativ geringere Rückresorption kommen schwangerschaftsspezifische Veränderungen in Frage: 1. Eine Erhöhung der extrazellulären Flüssigkeit, 2. die Erhöhung der glomerulären Filtrationsrate (GFR) und 3. die durch die vermehrte Natrium-(Na)-Reabsorption reduzierte Mg- und Ca-Reabsorption.

Summary

The magnesium (Mg) and calcium (Ca) excretion in the urine during pregnancy was determined in order to examine the reason for the decrease in the magnesium plasma level during pregnancy, a decrease which was shown to correlate with the diminished Mg-level in the myometrium. 24-hour urine and blood samples were taken from seven pregnant volunteers once every two weeks. The Mg was determined in the urine and plasma by using atom absorption spectrometry and the Ca was determined by colorimetry. The clearances were calculated. A 25 % increase in Mg-excretion to 4.78 mmol/24 h ($p<0.05$) was shown. The Mg-plasma level diminished by 25 % to 0.70 mmol/l ($p<0.01$). The Mg-clearance increased by 41 % to 4.57 ml/min ($p<0.05$). Already in the first trimester the Ca-excretion increased by 41 % to 4.86 mmol/24 h ($p<0.05$). The Ca-plasma concentration diminished by 12 % to 2.16 mmol/l ($p<0.001$). The Ca-clearance increased by 123 % to 2.03 ml/min ($p<0.02$). The increased Mg-excretion in the urine is therefore probably one of the reasons for Mg-deficiency. The following changes associated with pregnancy are to be considered as reasons for the relatively low reabsorption: 1. The increase in extracellular fluid, 2. the increase in glomerular filtration rate (GFR), and 3. reduced Mg and Ca-reabsorption due to increased sodium (Na) reabsorption.

Résumé

Les excrétions de magnésium (Mg) et de calcium (Ca) urinaires ont été étudiées au cours de la grossesse dans le but de rechercher les raisons de la baisse gravidique du Mg plasmatique, réduction correlée avec la baisse du Mg myométrial. Des prélèvements des urines de 24 h et du sang ont été effectués chez 7 femmes enceintes volontaires, chaque 2 semaines. Le Mg a été déterminé par spectrométrie d'absorption atomique et le Ca par colorimétrie. Les clairances ont été calculées. Un accroissement de 25 % de la magnésurie à 4,78 mmol 24 h ($p<0,05$) a été observé. Le taux de Mg plasmatique est réduit de 25 % à 0,70 mmol/l ($p<0,01$). La clairance du Mg augmente de 41 % à 4,57 ml/min ($p<0,05$). L'excrétion calcique augmente de 41 % pendant le 1er trimestre à 4,86 mmol/24 h ($p<0,05$). La concentration de Ca plasmatique diminue de 12 % à 2,16 mmol/l ($p<0,001$). La clairance du calcium augmente de 123 % à 2,03 ml/min ($p<0,02$). L'augmentation de la magnésurie est donc probablement une des raisons de la déficience magnésique. Elle peut provenir: 1. d'une augmentation des liquides extra-cellulaires, 2. d'une augmentation de la filtration glomérulaire, et enfin, 3. d'une réabsorption réduite de Ca et Mg due à une réabsorption accrue du Na.

Introduction

The observation that premature contractions can be reduced partly by administering Mg (*Spätling* 1981), drew attention to the role of Mg in pregnancy. As more precise methods of analysis such as atom absorption spectrometry became more wide-spread, it became feasible to correlate the data from these analyses to clinical manifestations. *Baltzer* and *Daume,* 1976, and others (*De Jorge* et al., 1965, and *Brockerhoff* et al., 1981) observed a reduction in Mg-plasma level particulary at the beginning of pregnancy. The Mg-plasma level reduced consistently and over a long period of time seems to influence growing tissues because it could be shown that the Mg-concentration of the uterus musculature diminished during the course of pregnancy (*Spätling* et al., 1983). Although the Mg-requirement of the uterus and foetus is not insignificant, it is unlikely that consistently low Mg-plasma values can be explained simply in these terms. The hypothesis established for the present study therefore was that urinary Mg-excretion increases during pregnancy. For this purpose, urinary Mg-excretion, Mg-clearance and Mg-plasma levels were measured during normal pregnancy and compared to the corresponding Ca-values.

Materials and methods

Seven volunteers aged 17 to 36 ($\eta=26$) participated in the study. Four of the women had their first child, two their second and one her third. They joined the study between their sixth and one her third. They joined the study between their sixth and twelfth week of pregnancy. 24-hour urine was collected in polypropylene containers every 2 weeks until delivery between the 34th and 40th week of pregnancy. The final examination placed between 6 and 8 weeks after delivery. Every time a blood sample was taken. The urine sample was shaken up, slightly acidified with HCl and an aliquod was used for analysis. Mg and Ca were determined by atom absorption spectrometry (Varian 875). Ca was measured with an analysis apparatus (Hitatchi 7059) implementing a colorimetric method (o-Kresolphthalein-Komplexon).

The amount of urine measured was used to calculate the clearance: c (clearance) = u (concentration in urine) / p (concentration in plasma) × v (volume of urine [ml/min]).

A linear regression of each parameter was determined from the data collected during the pregnancy of each patient. The differences between the regression values corresponding to the beginning and the end of gestation were compared by Wilcoxon rank test.

Results

The results are summarized in Table 1. The Mg-plasma level falls significantly during pregnancy by 15 % of the initial value to 0.70 mmol/l. The Mg-excretion rises by significantly 25 % to 4.78 mmol/24 h. Postpartal values decrease significantly to the levels during the first trimester. The Mg-clearance is increased by significantly 41 % to 4.57 ml/min. The value in non-pregnant women is at 3.23 ml/min is 5 % less than the levels during the first trimester. The Ca-plasma concentration falls during pregnancy by significantly 12 % to 2.16 mmol/l. In the first trimester it is already 6 % lower than the levels in non-pregnant women. During pregnancy it is decreased by further high significant 6 %.

The Ca-excretion rises already in the first trimester by significantly 41 %. An additional increase by further 44 % is not significant due to a large standard deviation. The Ca-clearance increases during pregnancy by significantly 123 % to 2.03 ml/min.

Table 1: Mg and Ca-plasma levels during pregnancy and post partum. The indices indicate the p values:
1 = $p < 0.05$, 2 = $p < 0.02$, 3 = $p < 0.01$, 4 = $p < 0.002$, 5 = $p < 0.001$

	n = 7	First Trimester	Third Trimester	Post partum
Mg	Plasma (mmol/l)	0.78 ± 0.05	0.70 ± 0.03^{3}	0.82 ± 0.05^{1}
	Excretion (mmol/24 h-Urine)	3.78 ± 0.77	4.78 ± 1.18^{1}	3.81 ± 0.92^{2}
	Clearance (ml/min)	3.39 ± 0.66	4.57 ± 1.13^{1}	3.23 ± 0.76^{3}
Ca	Plasma (mmol/l)	2.29 ± 0.06	2.16 ± 0.11^{5}	2.43 ± 0.19^{4}
	Excretion (mmol/24 h-Urine)	4.86 ± 2.59^{1}	6.37 ± 4.64	3.44 ± 2.32
	Clearance (ml/min)	1.47 ± 0.75^{1}	2.03 ± 1.49	0.91 ± 0.73^{2}

It is also important to observe the equilibrium of the antagonists Ca and Mg, shown in Table 2 as a quotient. During pregnancy the decrease of the Mg-plasma is somewhat larger than that of Ca demonstrated by slight rise in the quotient. Essentially the equilibrium between Ca and Mg remains substantial despite considerable changes in plasma concentration. The Ca/Mg quotient also changes very little in 24 h urine. Six to eight weeks after delivery, the quotient is considerably smaller than in the third trimester because less Ca than Mg is excreted. The same changes are reflected in the Ca and Mg-clearances.

Discussion

The hypothesis that urinary Mg-excretion increases during pregnancy is completely supported. The major result is that Mg-excretion increases by 25 %, despite the increased Mg-requirement during pregnancy.

The decrease in Mg-plasma level is more significant in this study than in others published up to now (*Baltzer* et. al., 1976, *Rathgen* et al., 1980). The Mg-excretion of 3.81 mmol/24 h is similar to that observed by *Leichsenring* et al. (1951). *Wacker* and *Vallee* (1960) found a Mg-excretion of 3.96 mmol/24 h in women. *Evans* and *Watson* (1966) observed that the Mg-excretion was significantly higher at 4.41 mmol/24 h, in in-patient women due to a correct urine sampling than in out-patient participants. Since the present study involved out-patient women, the absolute values for excretion and clearance may be even higher. Studies on changes during pregnancy have not been carried out.

In the present study, the decrease of 12 % in Ca-plasma values is considerably higher than the 5 % decrease found by *Brockerhoff* et al. (1981). The dilution of blood based on pregnancy is not in and of itself a sufficient explanation for the decrease of Mg and Ca in plasma because the same decrease would then be observed in other electrolytes.

Table 2: Calcium / Magnesium Quotient

	First Trimester	Third Trimester	Post partum
Ca / Mg Plasma	2.94	3.08	2.95
Ca / Mg 24 h-Urine	1.28	1.33	0.90
Ca / Mg Clearance	0.43	0.44	0.28

Na remains constant while potassium and chloride rise.

The changes in protein binding of Mg and Ca in pregnancy are difficult to interpret in this connection. If it is calculated only with the decrease in plasma protein concentration, a decrease of ionized Mg of 10 % and of Ca of 7 % is found none the less. It is unlikely that pregnancy does not affect the fraction of ionized Mg and Ca.

Heaney and *Skillman* (1971) observed a Ca-excretion of 3.49 mmol/24 h in non-pregnant women, similar to the 6 – 8 week postpartal value we found. *Davis* et al. (1970) found a slightly higher level of excretion at 4.55 mmol/24 h. Increased Ca-excretion in pregnancy with the exception of the last five weeks is described by *Heaney* and *Skillman* (1971). We are not able to confirm this finding in our study.

One reason for the increased Mg and Ca-excretion during pregnancy may be the 30 % increase in glomerular filtration rate (GFR) *(Sim* and *Krantz,* 1958). *Massry* (1981) writes that a constant increase of GFR could cause a significant decrease of Mg-plasma level. Another reason for the increased excretion of Mg and Ca could be the increase in extracellular fluid caused by pregnancy. *Massry* et al. (1969) describe a decrease in the tubular reabsorptive capacity caused by an increase of extracellular volume. The studies of *Di Bona* et al. (1971), demonstrating reduced Na-reabsorption after $MgSO_4$ infusion, clearly show how the reabsorptions of Mg, Ca and Na influences each other in the distal portion of the upward Henle loop. *Massry* et al. (1970) consider that the sites of reabsorption are limited and they demonstrate increased Mg, Na and Ca excretion in the urine after a $MgCl_2$ infusion. The increase in GFR due to pregnancy necessitates an additional Na-reabsorption of 10 000 mmol/24 h. It is therefore conceivable that this significant increase in Na-reabsorption occurs at the expense of Mg- and Ca-reabsorption, of which only 50 mmol/24 h, respectively 160 mmol/24 h, must be reabsorbed additionally during pregnancy.

The 3 mmol/24 h increase in Ca excretion that we measured corresponds to an approx. 10 mmol/24 h increase of Ca-reabsorption during pregnancy. No similar studies have been conducted on the balance of Mg, but the 25 % increase in Mg-excretion we measured seems to manifest itself in the cell Mg content of pregnant women. As mentioned before, we were able to show a decrease in the Mg-level of myometrial cells during the course of pregnancy (*Spätling* et al., 1983), but not a change in the Ca-level (*Spätling* et al., to be published).

The role of the parathyroid hormone, which is important in regulating Ca and Mg overall, is unclear because the level of this hormone increases only after the 24th to the 28th week (*Cushard* et al., 1972). The decrease in the Mg and Ca level, however, can be observed much earlier (*Brockerhoff* et al., 1981).

The present study provides evidence to support the assumption that a disturbance in the homoeostasis of electrolytes may also be responsible for difficulties during pregnancy. One possible reaction are premature contractions, for which *Fehlinger* et al. (1984) showed a correlation to imbalanced overall Mg-levels in a recently published study.

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